

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Hans Schreier et al.
Serial No: 10/528,783
Filed: 3/23/2005
Title: Medicament/Dosimeter Combination Packaging
Examiner: Ann Y. Lam
Art Unit: 1641

Commissioner for Patents
Alexandria, VA 22313-1450

RESPONSE TO OFFICE ACTION DATED 6/9/2009

In response to the office action dated 6/9/2009, applicant submits the following:

REMARKS

Rejection under 35 U.S.C. 103

Claims 8-15 stand rejected under 35 U.S.C. 103(a) as being unpatentable over *Webster et al.* (US 6,383,789) in view of *Coleman* (US 5,665,065) and further in view of *Depeursinge* (US 2003/0023345) or alternatively over *Webster et al.* (US 6,383,789) in view of *Price et al.* (US 2001/0051635), *Coleman* (US 5,665,065) and *Depeursinge* (2003/0023345).

Claim 8 sets forth the following features:

- a **dosimeter containing a medicament to be individually dosed**, wherein the dosimeter has a **chip and dispensing means** for the medicament,
- a **diagnostic indicator system for a patient-specific property** that is relevant for the action, side effect, interaction, metabolism, absorption, distribution, metabolism, and elimination of the medicament to be administered to a patient, wherein **the patient-specific property is a genetic property that is determined by gene expression testing**,
- wherein the diagnostic indicator system is comprised of a detector or chip with at least one reactive substance that when reacted with a bodily fluid provides information

regarding the physiological or pathological state of the patient, the dosage of the medicament, or both the physiological or pathological state of the patient and the dosage of the medicament,

- wherein **the dosimeter and the diagnostic indicator system are interconnected;**
- wherein the **information regarding the dosage is supplied to the dosimeter** for dispensing the medicament in accordance with the information regarding the dosage.

Webster et al. teach that it is generally known to identify by genotyping patients who are more prone to concentration dependent effects of a drug and who exhibit toxic side effects. Col. 2, lines 39-54, sets forth that:

“For example, polymorphisms expressing a non-functioning variant enzyme results in a sub-group of patients in the population who are more prone to the concentration-dependent effects of a drug. This sub-group of patients may show toxic side effects to a dose of drug that is otherwise without side effects in the general population. Recent development in genotyping allows identification of affected individuals.”

Accordingly, a patient is classified as belonging to the sub-group or not. The physician then is able to adjust the dosage of the medication accordingly so that the patient receives improved therapy. Col. 18, line 59, to col. 19, line 30, of *Webster et al.* also addresses the problem of a patient's genotype affecting the drug treatment and that pharmacogenomics enables the selection of effective compounds and effective dosage of such compounds. *Webster et al.* sets forth that:

“Accordingly, genetic polymorphism may lead to allelic protein variants of the drug-metabolizing enzyme protein in which one or more of the drug-metabolizing enzyme functions in one population is different from those in another population. The peptides thus allow a target to ascertain a genetic predisposition that can affect treatment modality. Thus, in a ligand-based treatment, polymorphism may give rise to amino terminal extracellular domains and/or other substrate-binding regions that are more or less active in substrate binding, and drug-metabolizing enzyme activation. Accordingly, substrate dosage would necessarily be modified to maximize the therapeutic effect within a given population containing a polymorphism.”

The reference therefore teaches that polymorphism-affected patients can receive a modified drug treatment in order to compensate for their different drug metabolism. This

is however not a patient-specific treatment but a treatment based on a classification into a sub-group of the population that is afflicted with polymorphism, i.e., the physician (see col. 2, lines 50-54, of *Webster et al.*) adjusts the dosage level to the treatment regime for polymorphism patients:

“As a result, their atypical metabolism and likely response to a drug metabolized by the affected enzyme can be understood and predicted, thus permitting the physician to adjust the dose of drug they receive to achieve improved therapy.”

The diagnostic tool provided by *Webster et al.* is provided for the physician who wants to make sure that his patient receives proper treatment. In order to make the right decision in regard to the level of medication to be administered, the physician will test the patient to determine whether the patient falls within the sub-group of critical patients. The physician or a lab carrying out his work orders will perform the test once. Based on the result - patient belongs to sub-group or not - the physician will prescribe the appropriate sub-group-based treatment. It is apparent from the disclosure of *Webster et al.* that genotyping is done by the physician and that a general (statistical) and not an individually adjusted medication regime is then prescribed.

The present invention is directed to a different and more individualized approach (page 2, lines 13ff):

“The use of the present invention is realized at three different levels:

1. as an analytical measuring unit before taking or dosing a medicament in order to define the (genetic) type of the patient and to derive therefrom a conclusion whether the patient is to be treated or not to be treated with a specific medicament or with a specific quantity of a medicament;
2. as a dosage metering unit during administration of the medicament in order to make available to the patient continuously the optimal dosage of the medicament;
3. as a monitoring measuring unit that continuously measures and documents the effect of a medicament and thus enables the patient and/or the physician to continuously monitor the success or failure of a medication.

Webster et al. only relates to a partial aspect of the above scheme: genotyping the patient. *Webster et al.* does not teach or suggest that genotyping (i.e., an analytical measuring unit) is to be combined with a dosage metering unit. As set forth in *Webster et al.*, the physician will determine the dosage to be applied and will provide the patient with a prescription to be filled and with a schedule in regard to how the medication is to be taken. The analytical measuring step is done once to determine whether the patient falls

into the sub-group of patients with polymorphism. The patient is then treated based on general non-individualized data. Nothing further is disclosed or suggested in regard to providing the patient with his individually adjusted optimal dosage of the medication based on the current state of the patient, diagnosed repeatedly and not just once at the onset of therapy, and his specific reaction to a medication. Please note Examples provided in the instant specification.

As set forth on page 4, lines 14ff, of the specification, the present invention is particularly directed to a combination as follows:

"In an ideal situation, test system and medicament form are interconnected with one another such that, by combining the chip with an appropriate chip on or in the medicament form, the latter indicates or releases the **optimal dosage of the medicament for the respective state based on the information** that is available without any action to be preformed by the patient or physician. Examples for this are a cassette that releases in accordance with the read-out information a certain quantity of capsules or tablets; a programmed droplet dispenser or cream dispenser; a subcutaneous injection, for example, with a "pen injector" that injects subcutaneously an amount of medication that is **precisely defined but variable depending on the individual information**; or a variable atomizer that atomizes according to the information a quantity of a substance that is then to be inhaled by the patient."

The instant specification sets forth on page 7, second to last paragraph, the advantages of the present invention:

"Based on the presented examples, it becomes clear that it is indeed conceivable to treat patients individually instead of according to a generalized treatment scheme that is based on statistic information but is too coarsely incremented. The consequence is an improved efficacy of the medicament that is adjusted individually wherein in the ideal situation also a significant reduction of side effects is observed because of the optimization of the dosage as well as of the dosage interval. This leads generally to a higher probability of curing as well as improved quality of life for the patient as well as to a reduction of the total costs and thus a positive economic effect for the patient or the health-care system."

Nothing suggests that according to *Webster et al.* the genotyping procedure is employed routinely in order to determine the patient's condition and/or the response to the medication and to make adjustments throughout the therapy based on the analytical results.

The examiner refers to *Coleman et al.* to show that it is known to provide a programmable medication infusion pump with sensor and a syringe for administering insulin based on blood glucose readings of the sensor. The examiner states that the *Coleman et al.* device is not limited to insulin. According to examiner it would therefore have been obvious to employ the device of *Coleman et al.* in combination with *Webster et al.*

As set forth above the *Webster et al.* reference discloses only that the genotype of a patient is determined and that based on the genotype the (statistical) medication level is determined. There is no suggestion in regard to repeatedly measuring and adjusting the medication level in response to gene expression so as to optimally administer the medication based on the current state of the patient throughout the therapy. This reference cannot teach repeatedly measuring and adjusting the medication level in response to gene expression so as to optimally administer the medication based on the current state of the patient. As *Webster et al.* only teaches that an adjustment of the medication is to be made based on the once determined sub-group status and a therapy regime is then set up, there is no need for further testing.

Coleman et al. shows a device for injecting insulin in accordance with the measured glucose level. This has nothing in common with the claimed combination package with an indicator system based on gene expression testing in order to determine a patient's individual fingerprint for selecting a proper medication and/or dosage for a therapy. Also, *Colman et al.* does not mention anything in regard to gene expression testing and, if anything, the reference suggests the use of blood chemistry readings in general (col. 1, lines 61-65), i.e., other readings of blood parameters than the glucose level could be the basis of administering a medication (e.g. thyroid hormone > thyroid medication; cholesterol/triglycerides > cholesterol-lowering drugs etc.). This reference cannot teach repeatedly measuring and adjusting the medication level in response to gene expression throughout a therapy so as to optimally administer the medication based on the current state of the patient throughout the duration of a therapy. As *Webster et al.* only teaches that an adjustment of the medication is to be made based on the initial determination whether the patient belongs to the sub-group at risk of side effects or toxic effects, there is not motivation to employ a device of *Coleman et al.*

Depeursinge only teaches that medication is contained in a programmable dispenser that can be manually or automatically locked and unlocked for dispensing based on stored parameters. This reference cannot teach repeatedly measuring and adjusting the medication level in response to gene expression testing so as to optimally administer the medication based on the current state of the patient throughout the therapy.

The combination of references *Webster et al.*, *Coleman et al.* and *Depeursinge* therefore cannot make obvious the invention as claimed in claim 8 and its dependent claims.

The examiner has further cited *Price et al.* in combination with *Webster et al.* to show that it is well known to combine diagnostic material and a medication in a kit. The diagnostic substance in the context of HIV infection enables the initial detection of the virus and subsequent treatment with the "effective inhibitory amount" of the one or more anti-HIV drugs. As in *Webster et al.* the diagnosis is limited to the initial determination of a sub-group -> HIV-infected. There is no teaching in regard to repeatedly measuring a patient-specific parameter and adjusting the medication level in response to gene expression testing so as to optimally administer the medication based on the current state of the patient. Like *Webster et al.* the reference to *Price et al.* only teaches that an adjustment of the medication is to be made only once based on the patient being classified as belonging to the sub-group. *Price et al.* also does not teach a patient-specific treatment - *Price et al.*, as all the other references, discloses a standard non-individualized treatment without taking into account specific reactions or conditions of the patient.

The combination of references *Webster et al.*, *Price et al.*, *Coleman et al.* and *Depeursinge* therefore cannot make obvious the invention as claimed in claim 8 and its dependent claims.

Reconsideration and withdrawal of the rejection of the claims under 35 USC 103 are therefore respectfully requested.

CONCLUSION

In view of the foregoing, it is submitted that this application is now in condition for allowance and such allowance is respectfully solicited.

Should the Examiner have any further objections or suggestions, the undersigned would appreciate a phone call or **e-mail** from the examiner to discuss appropriate

amendments to place the application into condition for allowance.

Authorization is herewith given to charge any fees or any shortages in any fees required during prosecution of this application and not paid by other means to Patent and Trademark Office deposit account 50-1199.

Respectfully submitted on September 7, 2009,

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